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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,919	03/26/2004	Thomas Wisniewski	57953/1211 (2003-11-WIS02	9386

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
03/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/810,919	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9,12,15,16 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7-9,12,15,16 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/7/8; 1/30/8*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 07, 2008 has been entered.

Response to Amendment

2. Claims 1 and 12 have been amended and claims 6, 10, 11, 17 and 21-26 have been cancelled as requested in the amendment filed on January 07, 2008. Following the amendment, claims 1, 4-5, 7-9, 12, 15-16 and 18-20 are pending in the instant application.

Claims 1, 4-5, 7-9, 12, 15-16 and 18-20 are under examination in the instant office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on January 07, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 4, 9, 12, 15 and 20 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating Alzheimer's disease by administration of amyloid peptides (proteins of SEQ ID NO: 2, 3 and 4), does not reasonably provide enablement for the full scope of the treatment and prevention of Alzheimer's by administration of an agent which inhibits interaction between amyloid-β peptide and apolipoprotein E for reasons of record in section 6 of Paper mailed on April 26, 2007. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant traverses the rejection on the premises that, "[t]he inhibition profile of Aβ12-28P against apolipoprotein E/amyloid-β peptide interaction is set forth in Figure 3 of the present application and further described in Example 15 […] Furthermore, inhibition of the apolipoprotein E/amyloid-β peptide interaction at the site on apolipoprotein E which binds to Aβ 12-28P appears to be nontoxic, because it does not inhibit any physiological reaction (like blocking amyloid β secretase, which serves multiple functions) and does not cause an autoimmune response (like the vaccine whose phase II clinical trial was stopped due to morbidity and mortality). Present Application, at pg. 5, lines 8-15" (pp. 4-5 of the Response). Applicant further submits that, "[w]ith this guidance, a person of ordinary skill in the art can develop other agents, such as proteins or peptidomimetics, non-proteinaceous agents, and modified proteins, using well known techniques, as set forth in the present application". Applicant's arguments have been fully considered but are not persuasive for the following reasons.

Applicant's invention is predicated on finding that administration of Aβ12-28P was beneficial with respect to reduction in amyloid plaque formation in transgenic mice and increase

of cell viability in culture. Based on the data obtained with Aβ12-28P, Applicant proposes a method of treatment of Alzheimer's disease by administration of an agent, which (1) binds to a site of apolipoprotein E that binds to SEQ ID NO: 4, and (2) inhibits interaction between amyloid-β peptide and apolipoprotein E. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification (see MPEP 2111 [R-1], which states that claims must be given their broadest reasonable interpretation

"During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the claimed method is that it allows treatment of Alzheimer's disease by administration of an agent, which is defined in the instant specification and recited in the claims as an "agent [which] (1) binds to a site of apolipoprotein E that binds to SEQ ID NO: 4, and (2) inhibits interaction between amyloid-β peptide and apolipoprotein E". The specification provides one example of an agent that meets the limitations of the claims and proposes an assay to practice, discover and develop agents, "such as proteins or peptidomimetics, non-proteinaceous agents, and modified proteins" (p. 5 of the Response),

which would satisfy the description and functional characteristics of the agent intended to be administered for clinical purposes. This situation is directly analogous to the one described in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). When claims depend on a recited property (*i.e.*, agent that binds and inhibits), a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the discloses at most only those known to the inventor. This appears to be the instant case and the claims are not commensurate in scope with the specification. In view of the absence of teachings and lack of reasonable expectation of successful results, it would require significant amount of undue experimentation for a skilled practitioner to research and discover for himself which agents that meet the limitations of the claims are suitable for administration to treat Alzheimer's disease.

Thus for reasons of record explained in the previous office communication and reasons set forth above, the instant rejection is maintained.

7. Claims 1, 4, 9, 12, 15 and 20 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 4, 9, 12, 15 and 20 encompass methods, which specifically require the use of an agent to be administered for treatment of Alzheimer's disease. The claims do not require that the agent possesses any particular conserved structure or other disclosed distinguishing feature. Thus, the claims encompass a genus of molecules that is defined only by ability to "(1) bind[s] to

a site of apolipoprotein E that binds to SEQ ID NO: 4, and (2) inhibit[s] interaction between amyloid-β peptide and apolipoprotein E". However, the instant specification fails to describe the entire genus of agents, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of one group of agents that satisfy the limitations of the claims, amyloid-β peptides. The claims, however, are drawn to agents that are described by their binding and inhibiting abilities toward certain molecules and molecular interactions. Thus, the claims are not limited to a molecule with a specific chemical structure or particular class of molecules with a common function. The claims only require the agent to satisfy the characteristics of the "(1) bind[ing] to a site of apolipoprotein E that binds to SEQ ID NO: 4, and (2) inhibit[ing] interaction between amyloid-β peptide and apolipoprotein E". The specification only describes amyloid-β peptides and fails to teach or describe any other agent which lacks the structure of β-amyloid peptide and has the activities possessed by the agent as currently claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of desired properties in the form of functional limitations. There is not even identification of any particular portion of the structure that must be conserved or region that is

specifically responsible for the desired function. The specification does not provide a complete structure of those agents that ""(1) bind[s] to a site of apolipoprotein E that binds to SEQ ID NO: 4, and (2) inhibit[s] interaction between amyloid-β peptide and apolipoprotein E" and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the encompassed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only amyloid-β peptides, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4-5, 7-9, 12, 15-16 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Schenk et al. 1999, WO 99/27944.

Claims 1, 4-5, 7-9, 12, 15-16 and 18-20 are directed to methods of treatment of Alzheimer's disease and inhibiting accumulation of amyloid-β peptide deposits by administration of an agent, which is an amyloid peptide (SEQ ID NO: 2, 1-43), fragment thereof (SEQ ID NO: 3, 12-28) or modified amyloid peptides. Document of Schenk discloses methods of treatment of amyloidogenic diseases by administration of Aβ, its fragments and modified embodiments thereof (see abstract and the whole document), thus fully anticipating the instant invention.

Allowable Subject Matter

10. Subject matter limited to a method of treatment of Alzheimer's disease by administration of a protein consisting of SEQ D NO: 4 is free of prior art and enabled.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

March 05, 2008

/Olga N. Chernyshev, Ph.D./
Primary Examiner, Art Unit 1649